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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,800	11/13/2006	Dieter Reif	50187	5864

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EXAMINER	
BERRIOS, JENNIFER A	

ART UNIT	PAPER NUMBER
1619	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,800	REIF ET AL.	
	Examiner	Art Unit	
	Jennifer A. Berríos	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *21-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. Applicant's Response and Amendments filed 3/4/2010 are acknowledged and entered. Claims 21-32 are withdrawn pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention. Claims 1-20 are currently pending and under examination. This Office Action is NON-FINAL.

Response to Arguments

Rejections/Objections Withdrawn

2. The rejections of claims 12 and 16 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, are withdrawn in light of Applicant's amendments.

3. Applicant's arguments, filed 7/27/2009, with respect to the rejections of claims 1-20 under 103(a) as being unpatentable over DE 29922585 and Beam (WO 02/083194) have been fully considered and are persuasive. Therefore, the rejections have been withdrawn. However, upon further consideration, new grounds of rejection are set forth below based on these references and newly cited prior art references.

New Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-2, 7, 12, 13-15 and 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over DE 29922585, Beam (WO 02/083194) and Starling et al (US 6,210,715, issued: 4/3/2001).

DE 29922585 teaches a bone defect filler or a bone formation agent with interconnecting micropores with an average size in the range of 0.5-10 μm (Pg 5) (compare instant claims 1 and 2). The sintered body has a total porosity of 60 vol%, micropores with an average size of 5 μm and macropores with an average size of 500 μm, but can range from 50-1000 μm (Pg 6 and 8). The macropores show a typical polyhedral shape over the entire size range (Pg 6). However, the choice of shape is a preferential choice that is a results-effective variable which can be optimized. Absent evidence to the contrary one of ordinary skill in the art would clearly recognize that the change in shape of the pores would not affect the functional ability of the claimed composition. The choice of pore shape amount to nothing more than routine experimentation that can be optimized on an individual basis (see *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977; and *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980)). Additionally, it would have been obvious to one of ordinary skill in the

art at the time of the invention to select an appropriate shape required to achieve a desired set of results. See *In re Dailey, 357 F.2d 669, 149 USPQ 47 (CCPA 1966)* (holding that the configuration of the claimed disposable plastic nursing container was a matter of choice which a person of ordinary skill in the art would have found obvious absent persuasive evidence that the particular configuration of the claimed container was significant.) and *Tronzo v. Biomet*, 156 F.3d at 1158-59, 47 USPQ2d at 1833 (Fed. Cir. 1998) (claims to generic cup shape were not entitled to filing date of parent application which disclosed "conical cup" in view of the disclosure of the parent application stating the advantages and importance of the conical shape), and MPEP 2144.04(B).

With regard to the statistical distribution of the pores, it would have been obvious to one of ordinary skill in the art to distribute the pores as necessary to achieve the best result through routine experimentation. B-tricalcium phosphate is used as the bone defect filler and is preferably employed as a polyhedral granulate in granulated sizes between 0.1-10 mm. Although this is slightly above the required particle size range, it's obvious to one of ordinary skill in the art to alter and optimize the sizes of the particles in order to achieve a desired set of results (Pg 6). Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See also, MPEP 2144.05.

The pure phase B-tricalcium phosphate has an average particle size d50 < 10, thereby satisfying the limitation of a d50 values in the range of 5-20 μm.

Regarding claim 7, the bone defect filler is in the form of a polyherdral granulate in graduated sized between 0.1-10mm (claim 3).

Regarding claims 13 and 19, the bone defect filler as a molded sintered body, preferably has the shape of a cylinder, cuboid or a cube, all defined geometric designs.

Regarding claim 17: The bone defect fillers can be treated, as such it would be present on it's surface and/or pores, with an active agent , preferably antibiotics and/or growth factors suitable for bone defect healing (claim 6).

Regarding claims 18 and 20: These claims recite intended use and therefore have no patentable weight. As the limitations of claim 13 is taught above, the limitations of these claims have been satisfied. Furthermore DE '585 teaches that the bone defect filler can be machined into the form of an implant individually matched to a patient (claim 5).

DE '585 does not teach the bone defect filler to comprise an isotropic structure.

Beam teaches a biostructure for implantation, having bimodal pore sizes (pg 120 and claims 3 and 9), made out of tricalcium phosphate (pg 135 and claim 111), which can be treated with substances such as antibiotics, growth promoting substance, etc (Pg 134, claim 103). Furthermore Beam refers to a structure which can be isotropic (pg 10).

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to combine the teaching of DE '585 and Beam. Because both DE '585 and Beam teach biostructure for implantation it would have been obvious to one of skill in the art to substitute one method for the other to achieve the predictable results of creating a biostructure comprising a isotropic structure.

Regarding claims 14-15: Any pore with any kind of depth is inherently in the shape of a tube, furthermore the pores of DE '585 satisfy the diameter range of 0.5-2mm. With regards to the statistical and tubular porosity, DE '585 teaches that total porosity lies between 60-80 vol% (Pg 6).

DE'585 and Beam also fail to teach the structure to only comprise interconnecting pores having a pore size less than 10 microns.

With regard to the limitations of claim 1, reciting that the interconnected pore share in the porosity is limited to pore sizes less than 10um, the variability of interconnected pores (which the examiner reads as "channels") in terms of size and connectivity (interconnectedness) is routinely altered by changes in sintering temperature, as taught by the '715 patent. Changes in sintering temperatures to effect

a more highly closed-porosity composition with fewer and smaller interconnected pores (channels) is taught by the '715 patent in Examples 3, 6, and 10. These sintering temperature ranges are taught in the instant specification at p.15. Temperatures are results-effective variables which can be optimized. In the case of adjusting the sintering temperature to effect a more dense composition with smaller pore sizes and interconnected pore (channel) sizes, one of skill in the art would clearly recognize that the sintering temperatures can be variable and could easily be optimized by one of ordinary skill in the art based on the need to affect pore size, channel size, and density of pores and channels, such that the composition comprises a more open or closed porosity, as taught by the '715 patent. In the instant case, optimization of sintering temperature to affect these physical compositional changes would amount to nothing more than routine experimentation that can be optimized. See *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977), *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980), *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955), *In re Hoeschele,* 406 F.2d 1403, 160 USPQ 809 (CCPA 1969), *Merck & Co. Inc. v. Biocraft Laboratories Inc.,* 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir. 1989) (cert. denied, 493 U.S. 975 (1989)), *In re Kulling,* 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990), *In re Geisler,* 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997), and MPEP 2144.05.

8. Claims 3-4 and 11-12 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over DE 29922585, Beam (WO 02/083194) and Starling et al (US 6,210,715, issued: 4/3/2001) as applied to claims 1-2, 7, 12, 13-15 and 17-20 above, and further in view of WO 92/21302.

DE '585, WO '194, and Starling teach all the limitations of claim 1, as set forth above, but do not teach the limitations further recited by claims 3, 4, 11, 12, and 16.

WO 92/21302 teaches an implant made of a porous, non-toxic material with a total porosity larger than 5% but not greater than 80% by volume. The implant is characterized in that it has three distinct pore sizes: 0.1-10 μm occupy 10-80% by volume; 10-50 μm occupy not more than 5% and 50-500 μm occupy from 5-40%.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of DE '585, WO 02/083194, and WO 92/21302 because all three references teach porous implants used for bone defect fillers or bone formation agents. One would be motivated to combine the references because by having porous implant with a distribution of pore sizes, in this case, one can combine a high strength and a capacity to meet high requirements as to a favorable situation for bone and tissue in-growth with an integrated interaction between soft and hard tissues, as taught, for example, by WO 92/21302 at pg 2, lines 22-26. Finally one of skill in the art would expect to be successful because the references all expressly teach porous biostructures comprising comprise calcium phosphate for implantation that comprise a plurality of pore size distributions.

Regarding claims 11, 12, and 16, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the instant invention was made to combine the cited prior art references and optimize the pore size distribution for the intended use of the claimed composition in order to achieve improved results through routine experimentation. Absent evidence to the contrary one of ordinary skill in the art would clearly recognize that the change in the pore size distribution would permit greater or lesser load-bearing of the implant and would promote greater or lesser in-growth of bone or tissue. These variables are optimizable based on the intended use application of the claimed composition. The choice of pore size distribution would amount to nothing more than routine experimentation that can be optimized on an individual basis (see *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977; and *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980)). Additionally, the prior art teaches a variety of pore size distributions depending on the application for which the implant is intended.

9. Claims 5, 8-10 and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over DE 29922585, Beam (WO 02/083194), Starling et al (US 6,210,715, issued: 4/3/2001) and WO 92/21302 as applied to claims 3-4 and 11-12 above, and further in view of US 6,521,246.

DE '585 / WO 02/083194 / Starling/WO/ 9221302 teach as set forth above, and teach the bone formation agent, but do not specifically recite the characteristics of the granulates of the bone formation agent.

The '246 patent teaches inorganic shaped bodies useful for bone grafting materials, cell growth scaffolds, drug delivery and more. It also teaches the methods of producing said inorganic bodies (column 1, lines 24-28). The '246 patent also teaches that these inorganic bodies can be formed into virtually any geometric shape (column 4, lines 2-3), although a uniform one is preferable, as suggested by the '246 patent claims 1, 14 and 22. The '246 patents goes on to teach that the uniform shaped body comprising meso-, micro-, and macroporous calcium phosphate, which comprises beta-tricalcium phosphate, is in the shape of a tube, block or sphere. The '246 does not explicitly state the amount of beta-tricalcium phosphate present in the inorganic material, but one of skill in the art would understand that a substantial amount necessary to perform the functions (bone grafting, cell growth, etc) were present.

It would have been *prima face* obvious to one of ordinary skill in the art to combine the teachings of the '246 patent with teaching of DE '585, WO 02/83194, and WO 92/21302 because they are drawn to compositions comprising bone formation agents that permit cell in-growth. "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). One of skill in the art would be motivated the prior art reference because the embodiments of the '246 patent (beta-tricalcium and the geometric shapes of the inorganic body) teach large varieties of shaped bodies that can be widely used in surgery, laboratory, and industrial processes and one of skill in the art would know that it's obvious to modify the shape of the biostructure in order to meet the desired needs (see abstract of the '246 patent). Finally, one of ordinary skill in the art would be motivated to combine the above teaches, because all teach biostructures with a distribution of pore sizes (2-3) and the biostructure comprising tricalcium phosphate, for the use of bone grafting, tissue

growth, and more. Applicant's attention is also drawn to *In re Dailey,* 357 F.2d 669, 149 USPQ 47 (CCPA 1966) (holding that the configuration of the claimed disposable plastic nursing container was a matter of choice which a person of ordinary skill in the art would have found obvious absent persuasive evidence that the particular configuration of the claimed container was significant.), *Tronzo v. Biomet*, 156 F.3d at 1158-59, 47 USPQ2d at 1833 (Fed. Cir. 1998) (claims to generic cup shape were not entitled to filing date of parent application which disclosed "conical cup" in view of the disclosure of the parent application stating the advantages and importance of the conical shape, and PEP 2144.04(B).

10. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over DE 29922585 and Beam (WO 02/083194), Starling et al (US 6,210,715, issued: 4/3/2001), WO 92/21302, and US 6,521,246 as applied to claims 5, 8-10 and 18-20 above, and further in view of Trisi et al (J Periodontics Restorative Dent 2003: 23:69-77), previously cited of record.

De '585, WO 02/083194, Starling, WO '302, and US '246 teach as set forth above, but do not teach limitations of claim 6.

Trisi *et al* teaches the effect of pure phase beta-tricalcium phosphate in bone regeneration. It teaches that pure phase beta-tricalcium phosphate is characterized by a ≥ 99 purity of the beta isomer. This material is more rapidly and predictably resorbed and replaced by newly formed bone without any residue (pg 70, paragraph 4).

It would have been *prima face* obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of De '585, WO 02/083194, Starling, WO '302, and US '246 and Trisi *et al.,* because they are drawn to compositions comprising bone formation agents that permit cell in-growth. One of ordinary skill in the art would have been motivated to combine the references because by using pure phase beta-tricalcium phosphate in the bone formation agent, the agent would be more rapidly resorbed and replaced by newly formed bone, therefore enhancing the function of the bone formation agent. Finally one of skill would expect to be successful because both teach agents used for bone formation and regeneration that comprise mainly calcium

phosphate. "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Conclusion

No claims are allowable.
This Office Action is NON-FINAL.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer A. Berríos whose telephone number is (571)270-7679. The examiner can normally be reached on Monday-Thursday: 7:00am-4:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571) 270-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JAB/
Examiner, Art Unit 1619

/Cherie M. Woodward/
Primary Examiner, Art Unit 1647